Increasing the endogenous mesenchymal stem cells to the bone surface to treat osteoporosis

Grant Award Details

Increasing the endogenous mesenchymal stem cells to the bone surface to treat osteoporosis

Grant Type: Disease Team Therapy Planning I

Grant Number: DR2-05302

Investigator:

Name:	Nancy Lane
Institution:	University of California, Davis
Type:	PI

Disease Focus: Bone or Cartilage Disease

Award Value: $107,750

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Grant Application Details

Application Title: Increasing the endogenous mesenchymal stem cells to the bone surface to treat osteoporosis

Public Abstract:

Although most individuals are aware that osteoporosis is disease of increased bone fragility that results from estrogen deficiency and aging, most are unaware of the high risk and cost of the disorder. It is estimated that close to 30% of the fractures that occur in the United States each year are due to osteoporosis (Schwartz & Kagan (2002). California, with one of the largest over-age-65 populations, is expected to double the fracture rate from 1995 to 2015 (Schwartz & Kagan 2002). One study places the cost per year in osteoporotic fractures at 2.4 billion dollars (Schwartz & Kagan 2002), establishing it as one of the highest health care costs for older individuals. The prevalence of osteoporosis is projected to increase with increasing lifespan globally both from age related bone loss and from secondary causes of bone loss including inflammatory diseases and cancer. In additional, medications used for the treatment of cancer and inflammatory diseases can also induce bone loss. Current treatment of osteoporosis is focused on agents that prevent further bone loss such as the bisphosphonates or selective estrogen modulators. The only bone growing agent that is approved by FDA is the protein, hPTH 1-34, which requires two years of daily injections and is only effective in about 60% of treated individuals.

We have developed a small molecule, LLP2A-Alendronate that augments the homing of endogenous mesenchymal stem cells (MSCs), the cells that have the potential to grow bone tissue, to the bone surface and form new bone. Therefore, we plan to file IND in the next sin months and we will perform two clinical trials to test its safety and efficacy in two clinical trials in the next fours years.

Yrs. 1-2: Phase I clinical trial. To determine if LLP2A-Ale is safe when used in patients with osteoporosis. After this phase I study, our research group will decide on two or three doses of LLP2A-Ale and two dosing regimens and will perform a phase II clinical trial.

Yrs. 3-4: Our phase II clinical trials will evaluate the efficacy of LLP2A-Ale in patients with osteoporosis The primary endpoint will be bone mineral density measured by DEXA of the lumbar spine and hip and biochemical markers of bone turnover, also calciotrophic hormones of bone metabolism (Vitamin D, FGF23, Sclerostin, IGF-1,and sclerostin,etc). Secondary clinical study endpoints will include a detailed assessment of the quantity of new bone formed and its distribution throughout the skeleton with XtremeCT, a new high-resolution 3 dimensional bone scan that allows regular follow-up measurements with software that automatically matches cortical and trabecular bone regions (SCANCO Medical microCT Systems) at 3 month intervals and bone biopsies performed at the iliac crest after treatment is completed. All the patients in the trials will be followed at 3 month intervals for 2 years.

Statement of Benefit to California:	Osteoporosis is a disease of the elderly that results from a process of age related bone loss that renders the bone fragile such that it breaks with very little force. Current osteoporosis treatments have relatively good efficacy in improving bone strength and reducing incident fractures, however these agents (anti-resorptive agents or the anabolic agent rhPTH (1-34) only reduce the risk of hip fractures by 40%, and require years of treatment to be effective. The goal of this project is to increase bone homing of the endogenous MSCs with a novel compound to form new bone as a novel treatment for osteoporosis. A compound that could cure osteoporosis with only 3-4 injections of an agent that mobilized MSCs to build bone would be highly competitive in this market as the efficacy of increasing bone mass and bone strength would be high and the risks in a very acceptable range. This agent would be effective in patients with primary osteoporosis defined by very low bone mass or low trauma fractures, in patients with secondary osteoporosis due to long term glucocorticoid treatment or after chemotherapy in both men and women and to augment peak bone mass in adolescents. The market potential for bone tissue regeneration is large, an estimated two million fractures and $19 billion in costs annually. By 2025, experts predict that osteoporosis will be responsible for approximately three million fractures and $25.3 billion in costs each year (publication from National Osteoporosis Function). The osteoporotic patients spend about $10 a month for the generic version of Fosamax, at the lower end, to about $80 a month for brand-name Fosamax or Actonel to $900 or more a month for Forteo (huPTH (1-34).A compound that could cure osteoporosis with only 3-4 injections of an agent that mobilized MSCs to build bone would be highly competitive in this market as the efficacy of increasing bone mass and bone strength would be high and the risks in a very acceptable range. Once validated in osteoporosis patients, this form of tissue regeneration will be useful for children in whom current osteoporosis medications is contraindicated, individuals who have had radiation to their skeletons, and to augment fracture healing in the elderly. The market potential for bone tissue regeneration is large as it is estimated that close to 1/3 of fractures that occur in the US each year are due to osteoporosis (Schwartz & Kagan (2002). California, with one of the largest over-age-65 populations, is expected to double the fracture rate from 1995 to 2015 (Schwartz & Kagan 2002). One study places the cost per year in osteoporotic fractures at 2.4 billion dollars (Schwartz & Kagan 2002), establishing it as one of the highest health care costs for older individuals. The prevalence of osteoporosis is projected to increase with increasing lifespan globally both from age related bone loss and from secondary causes of bone loss including inflammatory diseases and cancer.

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